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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,959	10/13/2000	James A. Bibb	600-1-257 CIP	8464

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EXAMINER	
SHUKLA, RAM R	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/687,959	Applicant(s) BIBB ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' amendments and response filed 9-30-02 and the declaration under 1.132 by Allen Fienberg have been received and entered.

2. Claims 1-15 have been cancelled.

3. New claim 22 has been entered.

4. Claims 16-22 are pending and under consideration.

Claim Rejections - 35 USC § 112

5. Claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record set forth in the previous office action of 3-29-02.

Response to Arguments

6. Applicant's arguments filed 9-30-02 have been fully considered but they are not persuasive. First applicants have argued legal standards in support of their argument by citing several court cases and argue that considerable amount of experimentation is permitted if it is routine, there is no need to set forth every minute detail regarding the invention, if the application defines the desired relationship, and that complex experimentation may be allowed if the art typically engages in such experimentation and finally, mere unpredictability of the result of an experiment is not a consideration. In response it is noted that the specification does not meet any of these criteria and the issues of functionally relationship, unpredictability of the state of the art (not experimentation), and important issues based on sound scientific reasoning and on review of the state of the art are not addressed by these court cases.

Next, applicants have argued in item 4b that specification provides sufficient guidance for identifying and using the agent in the claimed methods. It is noted

that applicants did not address the scientific issues raised regarding in vitro and in vivo correlations as evidenced by several research articles that reviewed the state of the art of the invention. They only stated that the declaration discusses US patent 5,777, 195. As noted in the previous office action, there is no evidence of record that a compound that inhibits the phosphorylation of Thr75 of DARPP-32 could treat any dopamine dysregulation related disease in view of the reports of Jaber et al and Fienberg et al. It is reiterated that at the time of the invention, role of agents that inhibited dopamine mediated signal transduction was not clear in the art and it was not routine in the art to treat diseases with such agents. Applicants have not provided any evidence that such methods were routine in the art.

In support of their arguments, applicants have provided a declaration by Allen A. Fienberg. The declaration has in paragraphs 5-8 reiterates what is present in the specification and therefore does not provide any new information or evidence. In paragraph 9-11, the declaration states that the rat model used in the specification was an art recognized model. First, there is no evidence of record to indicate that the rat model is a model for shizophrenia, Parkinson's disease, Tourette's disease, Huntington's disease, attention deficit hyperactivity etc. as discussed in the previous office action and however, there is no evidence that the rat model described in the specification is a model for any of these diseases. At best it is a model for chronic cocaine administration. The arts cited in the declaration only discuss cocaine use. Therefore, is no evidence in the art that an artisan could treat any dopamine dysregulation related disease such as schizophrenia, Parkinson's disease, Tourette's disease, Huntington's disease, attention deficit hyperactivity by delivering an agent that inhibited phosphorylation of Thr75-DARP-32, using the result in the animal model of the specification. Next the declaration states in paragraph 12-13 that using the teachings of the specification, an artisan could identify agents and treat any dopamine dysregulation, however, again there is no such evidence, except for arguments.

Next, in paragraph 14 and 15, the declaration stated that the results in brain slices were representative of results in vivo, however, there is no discussion of the

arts cited in the previous office action. In fact, it is not clear as to how the author in the Science article indicated that the in vitro results were not indicative of in vivo condition but in the declaration it the opposite. It is also noted that the articles listed in the declaration are not drawn to dopamine dysregulation, however, the article by Fienberg in Nature is about the same subject as that of the instant application. Therefore, the arts cited in paragraphs 14 and 15 are not representative of the same issue as discussed in the previous office action. Additionally, the arts cited for example, DB, support patent office's position that a very diverse types of physiological responses are mediated by DARPP-32 or CDK5 and therefore, an artisan can not treat every possible disease with inhibitors of these enzymes (see the discussion in the reference DB that discusses diverse results obtained with DARPP-32 mutant mouse on pages 1116 and 1117). In paragraph 16, applicants argue that it was routine in the art to test a potential agent in a mouse striatal brain slice assay and that subsequent testing in mouse could have been accomplished routinely, however, while the method steps would have been routine, the issue is a treatment of any disease related to dopamine dysregulation and it was not routine in the art to treat a disease, such as schizophrenia, Parkinson's disease, Tourette's disease, Huntington's disease. In paragraph, 18 of the declaration, it is stated that the agent would modulate dopamine signaling pathway, it does not matter whether the agent modulated or not other signal transduction pathways, however, this argument is not persuasive because while the agent may very well modulate dopamine signaling pathway, if there are several more pathways that it is going to modulate, how would an effective amount of the agent reach the dopamine signaling pathway. Further Dr Fienberg's argument that armed with such knowledge a skilled artisan could determine whether the effect be there in vivo, is not persuasive because the method is not for research, rather for treating a disease. In conclusion, the declaration does not provide any additional evidence that the claimed invention was enabled in light of the specification.

It is noted that the in the arguments presented by the applicants, Dr. Feinberg's declaration has been extensively discussed. In order to avoid

duplication, the applicants' arguments relating to the declaration by Feinberg will not be discussed again. Regarding the issue of D1 and D2 receptors, applicants' arguments have been found persuasive that both the pathways will be affected. Applicants' arguments in 4d and 4e do not provide any new evidence except for arguments.

In conclusion, it is noted that it was not routine in the art to treat a dopamine dysregulation condition using a CDK5 inhibitor, particularly in a situation where CDK5 is a cell cycle regulatory kinase and its inhibition would affect cell division in a general way and it is not clear what would be the outcome of such a treatment when given to an individual with symptoms of schizophrenia, Parkinson's disease, Tourette's disease, Huntington's disease, attention deficit disorder and drug abuse.

It is noted that it would have been undue experimentation for an artisan to have practiced the claimed method of treatment because neither the prior art nor the specification teaches as how to treat the claimed diseases in an individual by administering an inhibitor of DARPP-32 or CDK5 and such a method was not routine in the art and therefore, an artisan would not have been able to predict whether such a treatment would occur.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Tiffiany N. Tabb whose telephone number is (703) 605-1238.

Ram R. Shukla, Ph.D.

RAM R. SHUKLA, PH.D
PATENT EXAMINER